MR differentiation of adamantinous and squamous-papillary craniopharyngiomas.

Sartoretti-Schefer, S ; Wichmann, W ; Aguzzi, A ; Valavanis, A

Abstract: PURPOSE: To determine MR criteria for differentiating adamantinous from squamous-papillary craniopharyngiomas. METHODS: The MR imaging features of 42 histologically proved craniopharyngiomas (25 adamantinous, 15 squamous-papillary, and two mixed subtypes) were examined with multiplanar T2-weighted and noncontrast and contrast-enhanced T1-weighted imaging. Differences in the mR features of both subtypes were evaluated retrospectively. RESULTS: The adamantinous craniopharyngioma is a mixed solid-cystic or mainly cystic lobulated suprasellar or intrasellar/suprasellar tumor occurring in children and adults, typically with large nonenhancing hyperintense cysts on T1-weighted images. The squamous-papillary craniopharyngioma is a predominantly solid or mixed solid-cystic suprasellar tumor occurring in adults, appearing as a hypointense cyst on noncontrast T1-weighted images. Calcifications and recurrent tumors are more often observed in adamantinous tumors but can be seen in squamous-papillary tumors as well. Statistically significant parameters useful for differentiating the two tumor subtypes are the encasement of vessels, the lobulated shape, and the presence of hyperintense cysts in adamantinous tumors, and the round shape, the presence of hypointense cysts, and the predominantly solid appearance in squamous-papillary tumors. CONCLUSION: Craniopharyngiomas can be divided into two clinically, histologically different subtypes, which suggests a different pathogenesis of these two types of tumor.

MR Differentiation of Adamantinous and Squamous-Papillary Craniopharyngiomas

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PURPOSE: To determine MR criteria for differentiating adamantinous from squamous-papillary craniopharyngiomas. **METHODS:** The MR imaging features of 42 histologically proved craniopharyngiomas (25 adamantinous, 15 squamous-papillary, and two mixed subtypes) were examined with multiplanar T2-weighted and noncontrast and contrast-enhanced T1-weighted imaging. Differences in the MR features of both subtypes were evaluated retrospectively. **RESULTS:** The adamantinous craniopharyngioma is a mixed solid-cystic or mainly cystic lobulated suprasellar or intrasellar/suprasellar tumor occurring in children and adults, typically with large nonenhancing hyperintense cysts on T1-weighted images. The squamous-papillary craniopharyngioma is a predominantly solid or mixed solid-cystic suprasellar tumor occurring in adults, appearing as a hypointense cyst on noncontrast T1-weighted images. Calcifications and recurrent tumors are more often observed in adamantinous tumors but can be seen in squamous-papillary tumors as well. Statistically significant parameters useful for differentiating the two tumor subtypes are the encasement of vessels, the lobulated shape, and the presence of hyperintense cysts in adamantinous tumors, and the round shape, the presence of hypointense cysts, and the predominantly solid appearance in squamous-papillary tumors. **CONCLUSION:** Craniopharyngiomas can be divided into two clinically, histologically, and radiologically different subtypes, which suggests a different pathogenesis of these two types of tumor.

Index terms: Brain neoplasms, magnetic resonance; Craniopharyngioma; Sella turcica, neoplasms

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Craniopharyngiomas are intracranial epithelial neoplasms that occur in an intrasellar and/or suprasellar location in both children and adults (1–11). Two clinicopathologically and probably pathogenetically separate types (ie, the adamantinous and the squamous-papillary variants) of craniopharyngiomas have recently been distinguished (2, 3, 5–7, 10, 12–15).

The magnetic resonance (MR) appearance of craniopharyngiomas has been described in several reports (10, 14, 16–20). In this retrospective study we tried to determine the MR imaging criteria that differentiate adamantinous from squamous-papillary craniopharyngiomas. Also, on the basis of embryologic, immunohistochemical, and light/electronmicroscopic studies (21–23), we hypothesize the existence of a different pathogenesis for these two subtypes of craniopharyngioma.

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Materials and Methods

Forty-two patients with histologically proved craniopharyngiomas were studied retrospectively. In all patients, triplanar MR images were obtained on three different 1.5-T MR units using noncontrast T1-weighted imaging in 42 patients and contrast-enhanced T1-weighted imaging in 36 patients, as well as T2-weighted sequences in all patients. A bolus of 20 mL of gadopentetate dimeglumine was injected intravenously. The parameters of the T1-weighted images were 500–650/15–24/4 (repetition time/echo time/excitations). The T2 proton density–weighted images were obtained either as conventional spin-echo sequences with parameters of 2000/100,40/2 in 33 patients or as fast spin-echo sequences with parameters of 3500/95,20/2 in nine patients. The section thick-

TABLE 1: Location and MR characteristics of craniopharyngiomas

	No. of Patients (n = 42)	Tumor Type		
		Squamous-Papillary (n = 15), n (%)	Adamantinous (n = 25), n (%)	Mixed (n = 2)
Location				
Intrasellar/suprasellar	9	2 (13)	6 (26)	1
Suprasellar	33	13 (87)	19 (74)	1
MR characteristics				
Solid	2	2	. . .	. . .
Predominantly solid	8	5	3	. . .
Mixed solid/cystic	12	4	7	1
Predominantly cystic	11	2	9	. . .
Cystic	9	2	6	1
Predominantly solid	10	7 (47)	3 (11)	. . .
Mixed solid-cystic	12	4 (27)	7 (30)	1
Predominantly cystic	20	4 (27)	15 (59)	1
Additional characteristics				
Encasement of vessels	9	. . .	8	1
Mean tumor size, cm	42	4.2	4.9	4.9
Range, cm		(2.2–7.5)	(2.9–9.0)	(4.5–5.3)
Tumor shape				
Lobulated	26	4 (27)	20 (82)	2
Round	16	11 (73)	5 (19)	. . .

Note.—The percentage refers to either the adamatinous/mixed (27 tumors) or the squamous-papillary (15 tumors) craniopharyngioma subgroup.

ness ranged from 3 to 7 mm; the field of view varied from 160 to 210 mm.

Additional axial noncontrast and contrast-enhanced computed tomographic (CT) scans with a section thickness varying from 2 to 4 mm were obtained in five patients with adamantinous tumors and in two patients with squamous-papillary tumors. Twenty-five patients (11 female, 14 male) with a mean age of 24 years (range, 5 to 66 years; 16 patients less than 20 years old and nine patients more than 20 years old) had adamantinous tumors and two patients (13 and 21 years old, respectively) had a mixed adamantinous/squamous-papillary tumor. Fifteen patients (six female, nine male) with a mean age of 36 years (range, 3 to 61 years; two patients less than 20 years old) had a squamous-papillary tumor.

Follow-up examinations were performed in 18 patients (six patients with a squamous-papillary tumor and 12 patients with an adamantinous tumor). A single early postoperative study (within 2 months after surgery) was obtained in eight patients. A single late postoperative study was obtained in three patients (6, 8, and 20 months after surgery, respectively). Recurrent follow-up examinations (two to six imaging studies) were obtained in seven patients with intervals ranging from 2 to 60 months. Three patients with recurrent squamous-papillary tumors had had surgery at another hospital (therefore, no preoperative images were available).

The MR images were reviewed retrospectively and independently by two neuroradiologists. The following parameters were evaluated: location, size, and shape of the tumor; demarcation of the hypophysis within the sella; presence or absence of cystic and solid components of the tumor; signal intensity of cystic and solid components on T1-weighted images, on noncontrast and contrast-enhanced images, and on T2-weighted images; contrast enhancement pattern; presence of calcifications on MR and CT studies; and tumor recurrence on follow-up examinations.

Results

Tables 1 and 2 present the location and the typical MR imaging features of the two craniopharyngioma subtypes analyzed in this study. In tumors with an intrasellar/suprasellar location, the hypophysis was not visible and the sella was entirely filled with tumor. In some of the suprasellar tumors the tumor extended either downward through the diaphragm sellae into the intrasellar space (in two squamous-papillary and in five adamantinous tumors) or upward into the third ventricle, partly up to the foramen of Monro, thus leading to obstructive hydrocephalus (in six squamous-papillary tumors and in 16 adamantinous tumors). In both subgroups the number of tumors in a suprasellar location exceeded those in an intrasellar/suprasellar location; but in the patients with squamous-papillary tumors, the proportion of pure suprasellar

tumors was even higher than in the group with adamantinous tumors (Table 1).

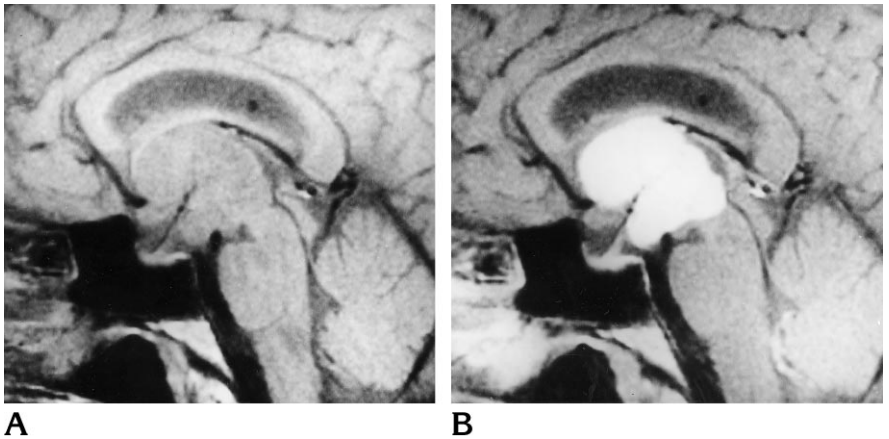
Squamous-papillary craniopharyngiomas usually were solid or predominantly solid (Fig 1) or mixed solid-cystic spherical tumors (Fig 2A and B; Table 1) in adults, occurring mainly in a suprasellar location (Table 1). On precontrast T1-weighted images the solid tumor parts were isointense or slightly hypointense and showed a strong but partly inhomogeneous enhancement (Figs 1 and 2). In four tumors, punctate hyperintense foci were visible within the solid tumor parts. On T2-weighted images, the solid tumor parts were inhomogeneously but strongly hyperintense. The rare cystic tumor parts were mostly hypointense on precontrast T1-weighted images (Fig 2A) and hyperintense on T2-weighted images, and had a thin peripheral contrast-enhancing rim on postcontrast T1-weighted images (Fig 2B; Table 2). Exceptionally, in two patients, the cystic tumor parts were hyperintense on precontrast T1-weighted images and either hyperintense or mixed (hyperintense and hypointense) on T2-weighted images. Calcifications (seen on preoperative CT scans in both squamous-papillary craniopharyngiomas but not seen on MR images) and recurrent tumors (in five cases, or 33%) were observed in sporadic cases (Fig 2C and D). In two patients, the tumor recurred after 24 and 36 months, respectively; in three patients, the exact time of tumor recurrence was not known. An encasement of arterial vessels within the subarachnoid space was not visible (Table 1).

Adamantinous and mixed tumors (the mixed tumors were assigned to the adamantinous tumor group during our study, because they appeared identical to the purely adamantinous tumors) were mostly cystic/predominantly cystic (Fig 3A and B) or, rarely, mixed solid-cystic (Fig 4A and B) lobulated tumors in children and adults, occurring in a suprasellar or intrasellar/suprasellar location (Fig 3A and B; Tables 1 and

TABLE 2: MR signal of tumor cysts before intravenous injection of contrast material (n = 40)

	No. of Patients	Tumor Type		
		Squamous-Papillary (n = 13), n (%)	Adamantinous (n = 25), n (%)	Mixed (n = 2)
T1 and T2 hyperintense	11	1 (8)	9 (37)	1
T1 hyperintense, T2 mixed	7	1 (8)	5 (22)	1
T1 hypointense, T2 hyperintense	17	11 (85)	6 (22)	. . .
T1 mixed (hyperintense/hypointense), T2 hyperintense	1	. . .	1 (4)	. . .
T1 mixed, T2 mixed	4	. . .	4 (15)	. . .
Hyperintense cysts	23	2 (15)	19 (78)	2
Hypointense cysts	22	11 (85)	11 (41)	. . .

Note—The percentage refers to either the adamatinous/mixed (27 tumors) or squamous-papillary (15 tumors) craniopharyngioma subgroup.



A B

Fig 1. Typical squamous-papillary tumor.

Sagittal noncontrast (*A*) and contrast-enhanced (*B*) T1-weighted MR images show a suprasellar solid tumor with a strong and slightly inhomogeneous enhancement. On the T2-weighted axial image (not shown) the tumor was inhomogeneously hyperintense.

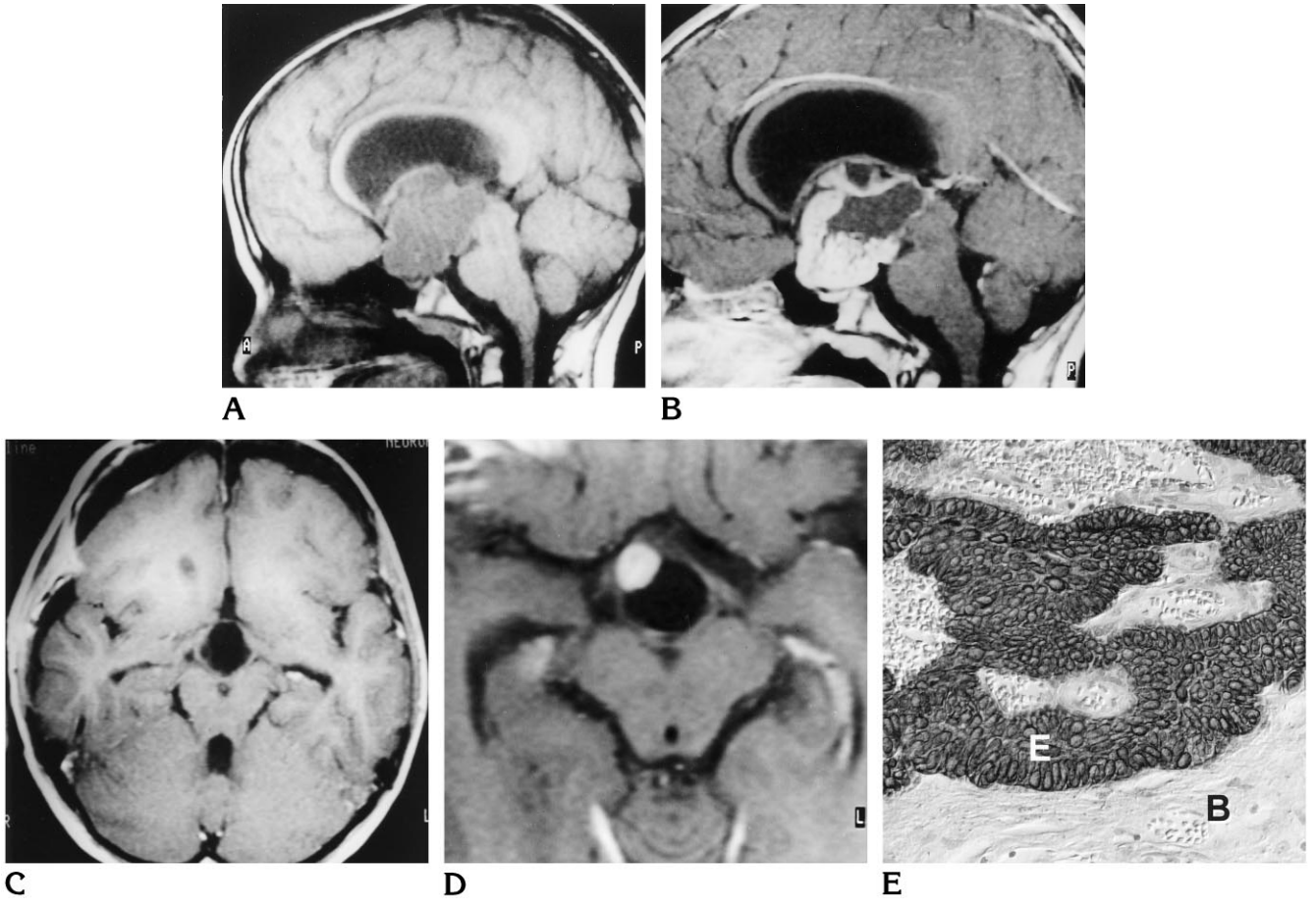


Fig 2. Mixed solid-cystic squamous-papillary tumor.

Preoperative sagittal noncontrast (*A*) and contrast-enhanced (*B*) T1-weighted MR images show a hypointense suprasellar tumor with a small punctate hyperintense focus on noncontrast image (not shown) with peripherally enhancing cystic areas and an inhomogeneously enhancing solid tumor part. No hyperintense cysts are present on noncontrast images.

Axial contrast-enhanced T1-weighted MR images 2 weeks (*C*) and 24 months (*D*) after surgery show a small solid enhancing recurrent tumor nodule along the left optic tract.

E, The histologic appearance of this tumor was characterized by papillary formations with fingerlike protrusions of neoplastic squamous epithelium (*E*) into the brain substance (*B*), immunostained with the antiepithelial antibody LU-5. The papillae of neoplastic epithelium include ectatic, blood-filled capillaries (hematoxylin-eosin, magnification ×200).

2). The solid tumor parts were isointense or slightly hypointense on precontrast T1-weighted images (Fig 4A) and showed a strong but inhomogeneous enhancement on postcontrast T1-weighted images (Figs 3B and 4B). Punctate hyperintense foci within the solid tumor parts were visible in five tumors. On T2-weighted sequences the solid tumor parts were inhomogeneously hyperintense and hypointense (Fig 4C and D). The very common, single or multiple tumor cysts were predominantly hyperintense (Figs 3A and 4A) or rarely hypointense on precontrast T1-weighted images and showed a minimal peripheral rim enhancement after injection of contrast material (Fig 3B; Table 2). The tumor cysts that were hyperintense on T1-weighted images were either hyperintense or mixed (hyperintense/hypointense) on T2-weighted images. An encasement of adjacent arterial vessels within the suprasellar cistern was present in one of three tumors (Fig 4A and B; Table 1).

The solid tumor parts in both tumor variants showed a strong but inhomogeneous enhancement and small or moderately sized necrotic nonenhancing areas (up to 2 cm diameter) on T1-weighted images (Figs 2B and 4B) and a strong but inhomogeneous hyperintensity on T2-weighted images.

Statistical evaluation of the significance of the various MR imaging parameters used for differentiating adamantinous from squamous-

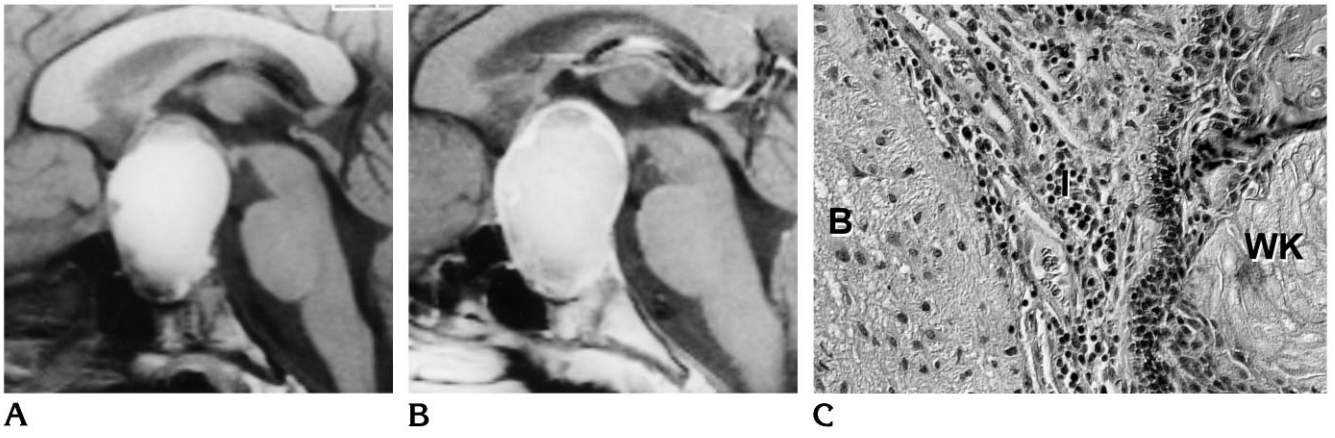


Fig 3. Typical adamantinous tumor.

Noncontrast (*A*) and contrast-enhanced (*B*) sagittal T1-weighted MR images show an intrasellar/suprasellar tumor with a hyperintense cystic peripherally enhancing mass and a small solid inhomogeneously enhancing portion.

C, The histopathologic pattern is characterized by the presence of wet keratin masses (*WK*) and inflammatory infiltrates (*I*). Note the sharp demarcation of the process to the brain parenchyma (*B*) (hematoxylin-eosin, magnification ×200).

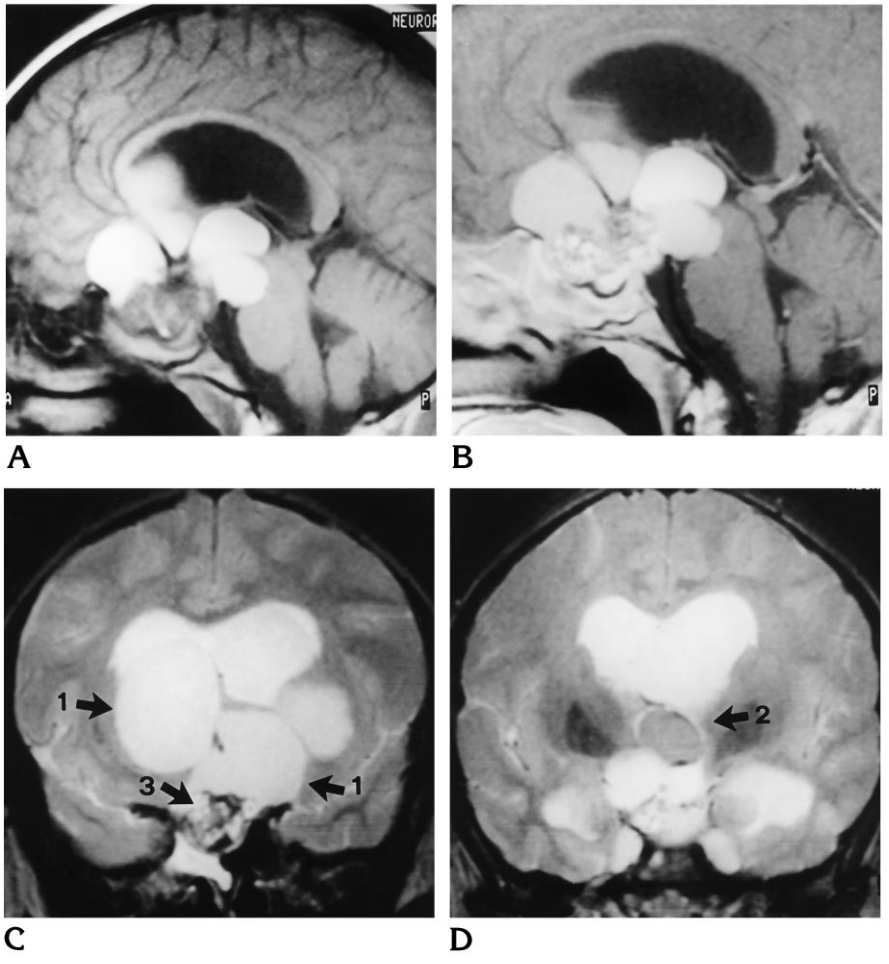


Fig 4. Noncontrast (*A*) and contrast-enhanced (*B*) sagittal T1-weighted MR images show a lobulated adamantinous tumor with multiple hyperintense cysts and a solid inhomogeneous mainly hypointense area with punctate hyperintense foci on the noncontrast image. The hyperintense cysts do not enhance after injection of contrast material; the solid tumor part enhances inhomogeneously. Encasement of the pericallosal artery and the basilar artery is present.

C and *D*, Coronal T2-weighted MR images show the cysts are either hyperintense (*1*) or hypointense (*2*). The solid tumor parts are inhomogeneously hypointense and hyperintense (*3*) owing to small hemorrhages and keratin deposits.

TABLE 3: Histopathologic differences between adamantinous and squamous-papillary craniopharyngiomas based on the World Health Organization's classification of brain tumors (2,22)

Histopathology	Adamantinous Craniopharyngioma (Mixed Solid-Cystic)	Squamous-Papillary Craniopharyngioma (Mainly Solid)
Displacement and attachment to adjacent vessels and cranial nerves	+	−
Calcifications	+	Rare
Encysted cholesterol-containing oil	+	−
Keratin nodules (wet keratin)	+	−
Cholesterol clefts	+	−
Necrotic debris and fibrosis	+	−
Keratin-positive squamous epithelium with:		
Peripheral cellular palisading	+	−
Stellate reticulum	+	−
Formation of papillae	−	+
Inflammatory reaction	+	−
Brain invasion	+++	+

papillary craniopharyngiomas was performed with the help of the Fisher's Exact Test for small populations of patients. We found no statistical significance between adamantinous and squamous-papillary craniopharyngiomas in terms of tumor location (ie, intrasellar/suprasellar versus suprasellar location, $P = .2943$). However, we did find statistically significant parameters, useful for differentiating between the two tumor subtypes, as follows: for the adamantinous tumors, the encasement of the subarachnoid arterial vessels ($P = .01$), the lobulated shape ($P = .00071$), and the presence of hyperintense cysts ($P = .00027$); statistical evaluation showed a tendency toward significance for the predominantly cystic appearance ($P = .04$); for the squamous-papillary tumors, the round shape ($P = .00071$), the presence of hypointense cysts ($P = .01$), and the predominantly solid appearance ($P = .01$).

Discussion

Craniopharyngiomas are epithelial neoplasms typically confined to the sellar and suprasellar region that arise predominantly in the first three decades of life, although they may occur in any age group. They account for 1.2% to 3% of all intracranial tumors, with an incidence of 0.5 to two new cases per million persons each year (1–3, 10).

Marked differences in clinical presentation and postoperative outcome between children and adults with craniopharyngiomas (1, 4–8) have prompted a thorough histologic review in these two patient groups, which has resulted in the separation of craniopharyngiomas into two clinically and pathologically distinct subtypes (ie, the adamantinous and the squamous-papillary variants) (2–3, 5, 8, 9, 12–14), which presumably represent two different clinicopathologic entities (2, 5, 6). Histopathologically, the two tumors can be reliably differentiated on the basis of various distinct histopathologic features as described in Table 3 (2, 3, 8, 10, 14, 24) (Figs 2E and 3C). The histologic combination of papillary and adamantinous tumor parts within the same neoplasm has been described in 15% of histologically proved tumors (14); however, these mixed tumors are clinically and radiologically similar to the purely adamantinous forms observed in our study. Therefore, the mixed tumors may be assigned to the adamantinous tumor group, because their appearance is similar to that of adamantinous tumors on MR images.

On MR images, differentiation of squamous-papillary and adamantinous tumors is suggested by the features summarized in Table 4. Typical features of a squamous-papillary craniopharyngioma include a predominantly solid or mixed solid-cystic spherical tumor in a suprasellar location in adults. The solid tumor parts have an inhomogeneous but intense enhancement, with small necrotic areas. The tumor cysts contain a watery liquid that is hypointense on T1-weighted images and hyperintense on T2-weighted images.

Recently, almost identical MR findings have been reported in squamous-papillary tumors (14, 25), except for a predominance of a cystic or mixed solid-cystic appearance in one of the

TABLE 4: Typical clinical and MR characteristics of adamantinous and squamous-papillary craniopharyngiomas

	Adamantinous Craniopharyngioma	Squamous-Papillary Craniopharyngioma
Location	Suprasellar	Intrasellar/suprasellar or suprasellar
Age	Children, occasionally adults	Adults
Tissue structure	Predominantly cystic†	Predominantly solid*
Tumor cysts on noncontrast T1-weighted images	Hyperintense cysts typical,* hypointense cysts possible	Hypointense cysts, if ever*
Tumor shape	Mostly lobulated*	Mostly spherical*
Encasement of subarachnoid arterial vessels	Yes*	No
Tumor recurrence	+++	+
Calcifications	+++	+

* These MR characteristics are statistically significant for differentiating between adamantinous and squamous-papillary craniopharyngiomas according to Fisher's Exact Test.

† These MR characteristics show a tendency toward statistical significance for differentiating between adamantinous and squamous-papillary craniopharyngiomas according to Fisher's Exact Test.

studies (14). However, of 48 squamous-papillary tumors reported in that study (14), only five were examined with MR imaging. The findings in the other study (25) mirror our results, with a predominance of solid tumors.

The adamantinous craniopharyngioma is a cystic or predominantly cystic lobulated tumor, often observed in an intrasellar/suprasellar location in children (25). On precontrast T1-weighted images, typically single or multiple hyperintense cysts with thin peripheral enhancing rims are present (25). On T2-weighted images, these cysts are either hypointense or hyperintense. According to our own findings as well as recently published results of neuropathologic and biochemical studies, these cysts contain various amounts of cholesterol, triglycerides, methemoglobin, protein, and desquamated epithelium (16–19, 26, 27). The signal intensity of these cysts is mainly influenced by a protein concentration greater than or equal to 90 g/L and the presence of free methemoglobin. The concentration of cholesterol and triglycerides, however, does not seem to change the signal intensity, because no change can be observed with the different lipid concentrations within the cysts (26). Occasionally, cysts with a watery fluid content that are hypointense on noncontrast T1-weighted images and hyperintense on T2-weighted images are observed in adamantinous tumors as well.

The solid tumor part enhances inhomogeneously on T1-weighted images, suggesting the possibility of small necrotic areas. The hypointense areas within the solid tumor parts on T2-weighted images represent areas with deposits of hemosiderin and keratin nodules (2, 24). Encasement of adjacent arterial vessels within the suprasellar cistern is a characteristic and specific feature of adamantinous tumors that has been described in reports of histologic findings as well (2, 3, 5, 15). This feature can be reliably depicted on MR images, as shown in our study (25). The punctate hyperintense foci on noncontrast T1-weighted images within the solid tumor parts in both adamantinous and squamous-papillary tumor groups are caused by histopathologically verified small hemorrhages (2, 24).

Despite these characteristic and specific differences in the MR features of both tumor groups, two squamous-papillary tumors had the above-mentioned MR characteristics of an adamantinous tumor. In one child (Fig 5) and in one adult, an intrasellar/suprasellar, mainly cystic tumor with a single large cyst, hyperintense on noncontrast T1-weighted images (Fig 5A) and inhomogeneously hyperintense on T2-weighted images, was observed. In one patient, calcifications were noticed on CT scans (Fig 5C). According to our study, these morphologic features are typical of adamantinous tumors, but in both cases the histologic specimen revealed a distinct squamous-papillary tumor. Two possible explanations may account for these discrepancies: the two tumors were probably histologically mixed tumors with clearly defined adamantinous and squamous-papillary components within the same tumor (14) but only the parts of the tumor containing the squamous-papillary component were sent out for histologic examination. These mixed tumors typically show the same MR features as the purely adamantinous tumors (as observed in

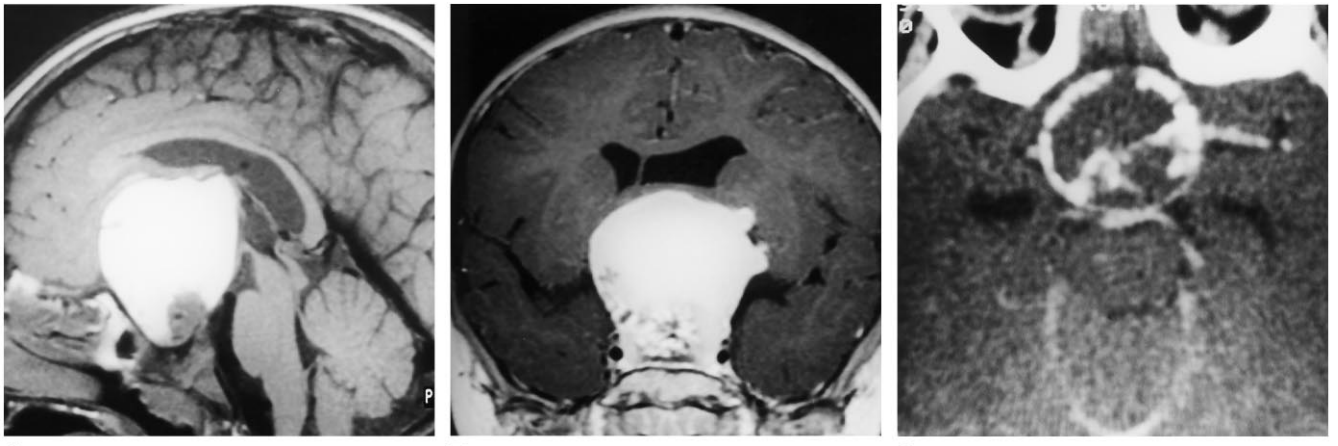


Fig 5. *A*, Noncontrast sagittal T1-weighted MR image shows a large intrasellar/suprasellar tumor with extension up to the foramen of Monro and associated hydrocephalus. A large hyperintense cyst and a small hypointense solid tumor are seen.

B, Contrast-enhanced coronal T1-weighted MR image of the hyperintense cyst shows a peripheral enhancing rim and inhomogeneous enhancement of the solid tumor parts.

C, Axial CT scan shows peripheral calcifications. Histologically, this tumor was a squamous-papillary tumor despite the features suggestive of an adamantinous craniopharyngioma.

two cases in our series). On the other hand, secondary degenerative changes in squamous-papillary tumors may also result in calcification in this tumor group. The presence of calcifications in squamous-papillary craniopharyngiomas has been confirmed in a recently published series of 56 surgically verified craniopharyngiomas of both subgroups (12, 13). Calcifications, therefore, are not a specific feature of the adamantinous tumors, as suggested in previous histologic reports, but occur in both tumor groups. Nonetheless, calcifications are still more frequent among adamantinous than squamous-papillary craniopharyngiomas (12–14, 16–24).

Recurrences of adamantinous craniopharyngiomas at a rate of 9% to 59% have been reported as late as 30 years after surgery, but no recurrence has been described in the squamous-papillary tumors in the older literature (2, 3, 5–8). In our retrospective study, recurrent tumors were detected in both the adamantinous and the squamous-papillary craniopharyngiomas. In three patients with squamous-papillary tumors, however, no preoperative or early postoperative MR images were available, and the patients first presented with a recurrent tumor at our institution after having had surgery at another hospital. Therefore, a distinction between recurrent or residual tumor was not possible. Two patients had had surgery in our neurosurgical department and preoperative as well as early and late postoperative MR images reliably proved the recurrence of a solid tumor after 24 and 36 months, respectively. On the preoperative MR images, one of these two lesions exhibited the morphologic features of an adamantinous tumor but histologically the tumor was diagnosed as a squamous-papillary craniopharyngioma. The other lesion showed the typical MR features of a squamous-papillary tumor on the preoperative MR images. We believe that recurrent tumors are rare in the squamous-papillary variant, but they may occur sporadically, a fact that is supported by recently published studies (12–14). Patients in both tumor subgroups had recurrent tumors, and in patients in whom the tumor had been totally resected, the recurrence rate was slightly less frequent in the squamous-papillary subgroup than in the adamantinous subgroup (not a statistically significant difference) (15). Subtotal resection predisposed to recurrence, regardless of pathologic subtype (12, 14).

According to older histopathologic reports (2, 3, 5, 6), the occasional appearance of small islands of tumor cells within adjacent normal brain tissue occurred only in patients with adamantinous tumors and was thought to be responsible for tumor recurrence in these patients. Recent data, however, show that brain invasion occurs both in adamantinous and squamous-papillary craniopharyngiomas (11, 12). The recurrence rate of both types of tumor probably depends not only on the presence of

brain invasion (15) but also on the extent of tumor resection.

The pathogenesis of craniopharyngiomas is controversial, but two major hypotheses concerning tumor development are available. According to the first hypothesis (4, 22, 23), the tumors arise from ectopic embryonic remnants of the craniopharyngeal duct, which connects the stomodeal ectoderm with the evaginated Rathke's pouch, which in turn forms the future adenohypophysis (Fig 6). A rotation of the adenohypophysis caused by different rates of cellular multiplication results in a spread of cell rests of the craniopharyngeal duct from the intrasellar space to the suprasellar region along the pituitary stalk. This may explain why craniopharyngiomas arise not only along the migration route of the craniopharyngeal duct, through the nasopharynx and the sphenoid sinus in rare cases (28–31), but also, mainly, in the intrasellar and suprasellar regions. The close topical embryologic relationship between the stomodeum and the lamina dentalis, which forms the future enamel organ of the teeth, accounts for the histologic similarity between the adamantinoma of the jaw, the keratinizing and calcifying odontogenic cyst (a special odontogenic tumor), and the adamantinous craniopharyngioma (2) and provides an explanation for the occasional development of real teeth within craniopharyngiomas (32–34).

The hypothesis relating the origin of the craniopharyngioma to remnants of Rathke's pouch is supported by various immunohistochemical and electron-microscopic studies: in adamantinous craniopharyngiomas, a secretory activity of epithelial cells lining the tumorous cysts results in the production of mucous. The mucin profile is similar to that produced by the oropharyngeal mucosa (22). Additionally, the fact that human chorionic gonadotropin is produced in pituitary glands, in pituitary adenomas, and in craniopharyngiomas, and that P-glycoprotein is produced in the pars intermedia of the hypophysis, in Rathke's pouch, and in craniopharyngiomas has also been used to suggest a common embryologic ectodermal origin (23).

According to the second hypothesis (Fig 7), craniopharyngiomas arise from squamous epithelial cells (35–37) in the pars tuberalis of the adenohypophysis (35). Human pars tuberalis cells represent mainly a subpopulation of gonadotrophs interspersed with a few corticotrophs

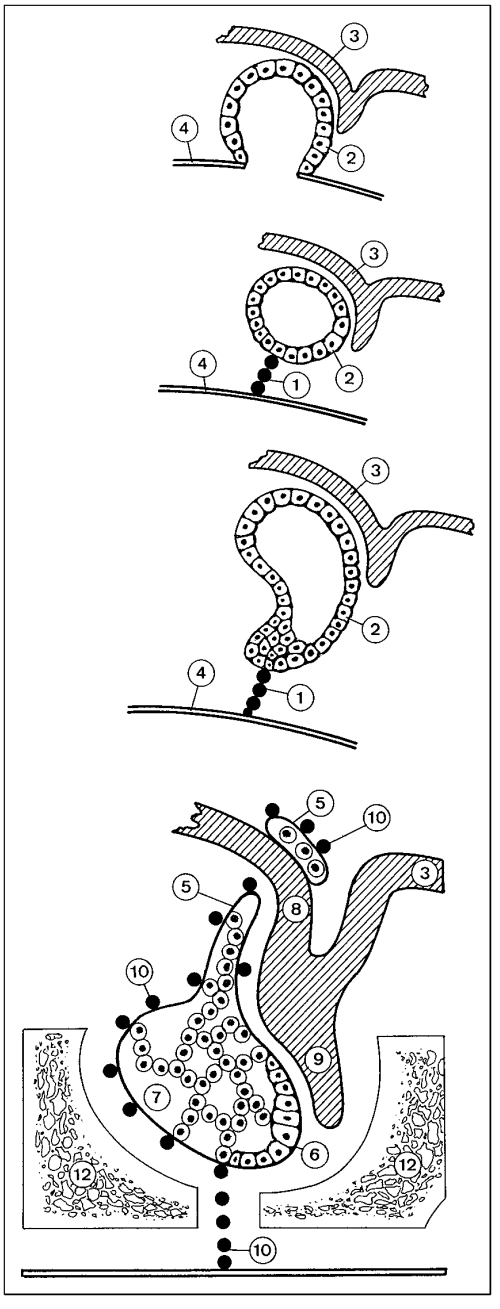


Fig 6. Proposed mechanism for the formation of an adamantinous craniopharyngioma. During embryogenesis, Rathke's pouch (*2*) forms an evagination of the stomodeum (*4*) adjacent to the lamina dentalis. Additionally, the diencephalon (*3*) has a caudal evagination, resulting in the development of the neurohypophysis (*9*). The cells of the craniopharyngeal duct (*1*), which initially connects Rathke's pouch with the stomodeum, subsequently show regressive changes. During the process of proliferation and rotation of the cells of Rathke's pouch—leading to the formation of the adenohypophysis, including the pars tuberalis (*5*), pars intermedia (*6*), and pars anterior (*7*)—cell remnants (*10*) of the craniopharyngeal duct are spread through the intrasellar and suprasellar region along the pituitary stalk (*8*) and are proposed to be the precursors of the adamantinous craniopharyngioma. (*12* indicates the sella turcica.)

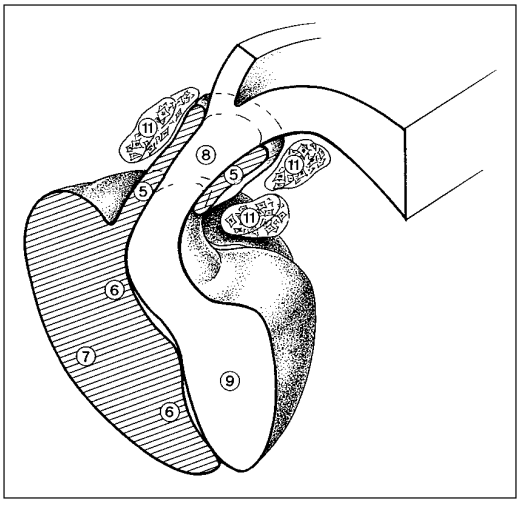


Fig 7. Proposed mechanism for the formation of a squamous-papillary craniopharyngioma. During embryogenesis, the pars tuberalis of the adenohypophysis (*5*) wraps around the pituitary stalk (*8*). Functionally inactive but hormone-producing and hormone-storing cells (FSH, LH, corticotropin) within the pars tuberalis undergo metabolic changes with increasing age. These metaplastic cells probably form the histologically observed keratin-positive squamous-cell nests (*11*), which are presumably precursors of the squamous-papillary craniopharyngioma.

and thyrotrophs that possess all organelles required for synthesis and storage of hormones but show ultrastructural features of functional inactivity. Immunoelectron microscopy shows follicle-stimulating hormone (FSH), luteinizing hormone (LH), and corticotropin in secretory granules. By light microscopy, squamous cell nests are positive for immunoreactive keratin and show evidence of hormone production in cells at their periphery. In some cases, cells of both keratin and hormones are detected. Because of this, a metaplasia of pituitary cells of the pars tuberalis resulting in the formation of the squamous cell nests is suspected. This concept is supported by several facts; namely, squamous cell nests rarely are found in patients under 20 years of age and they increase in frequency with age (36). They are not found in loci derived from the obliterated connection with the pharynx. The cells resemble those of clusters of pituitary cells (36). The demonstration of granulated hormone-containing gonadotrophs and corticotrophs at the periphery and within squamous nests of pars tuberalis indicates the derivation of the epithelial cells by metaplasia. The reason for the metaplasia, however, remains unknown. Additionally, craniopharyngiomas show positivity for various pituitary hormones (21). According to all these data it might be thought that the adamantinous craniopharyngioma arises from embryonic remnants of the craniopharyngeal duct and the squamous-papillary tumor from the squamous cell nests of the pars tuberalis of the adenohypophysis, thus resulting in a different clinicopathologic presentation and in a different MR morphology as described in our study.

The importance of a preoperative differentiation between adamantinous and squamous-papillary craniopharyngiomas is uncertain. According to older neuropathologic and neurosurgical studies, the postoperative outcome was thought to be much better for patients with squamous-papillary tumors than for patients with adamantinous tumors, and tumor recurrences were only reported in cases of adamantinous tumors (3, 5, 6, 15). Therefore, patients with adamantinous tumors had to be carefully informed about possible tumor recurrence. Recent studies (11, 12), however, have shown these common concepts to be only partially correct, because they have found, for example, no statistically significant difference in the tumor recurrence rate, in the postoperative outcome, and in the mortality rate between the two tumor groups (12, 14). The surgical procedure is not affected by a preoperative knowledge of the correct tumor diagnosis, because total removal of the tumor is desirable in order to produce a negative recurrence rate (12). The preoperative MR differentiation of these two tumor subgroups therefore remains primarily a scientific, although radiologically challenging, goal. Further histologic, clinical, and neuroradiologic studies are necessary to prove the real value of the preoperative distinction of these two subgroups.

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